REMARKS

Claims 1-14, 17, 19-24, 26, 27, 29, and 32 are pending in the present application. Claims 1-13, 21 and 22 have been withdrawn from consideration based on a restriction requirement.

Claims 14, 17, 19, 20, 23, 24, 26, 27, 29, and 32 remain under active consideration. Based on the comments made by the Examiner in the January 2, 2002 Office Action, it is respectfully submitted that the amendments made herein place this application in form for allowance.

Claim 31 has been canceled as being largely redundant of amended claim 14.

Claim 32 covers the use of the assay of the present invention to detect the occurrence and severity of stroke (cerebrovascular accident) in a patent; cerebrovascular accident and stroke are equivalent terms (see materials attached). Antecedent basis for this claim is found in claims 14 and 30, as originally filed, as well as at page 4, line 17-page 5, line 4 of the present application. Basis for the words "head" and "head trauma" is found at page 2, lines 6, 9, 12 and 14 of the present application.

By way of review, the present invention provides a quick and effective method for assessing in a patient whether there has been axonal damage resulting from a traumatic head injury (including a stroke), and the extent of that damage. Until now, there has been no effective, minimally invasive procedure for quickly determining that information which, of course, can be critical in an emergency room setting. In this method, a patient suspected of having such traumatic head injury, such as a stroke or a blow to the head sustained in a car accident, provides a sample of cerebrospinal fluid. The presence in that fluid of specific tau proteins are then determined using a monoclonal antibody raised against those proteins, and the levels of those proteins in the fluid are compared to control samples representing both damaged and undamaged states. This comparison yields information regarding whether there has been a traumatic head injury and the extent of that injury in the patient.

The objections raised by the Examiner in the Office Action will now be considered sequentially, referring to the paragraph numbers used by the Examiner.

Paragraph 8. The Examiner has rejected the claims, under the first paragraph of 35 U.S.C. § 112, contending that the terms "traumatic central nervous system injury" and "in the range of from about 30 to about 50 kDa" are not supported by the disclosure.

Claims 14 and 31 have been amended to utilize the phrase "traumatic head injury" in place of "traumatic central nervous system injury." Antecedent basis for this amendment is found page 2 of the present application where it refers to "head injury" (see lines 6 and 9), "head trauma" (see lines 12 and 14), and combines a discussion of head trauma and CNS injury (see line 18). The term "traumatic head injury" is a term well-known and well-accepted in the art – see the attached materials from the U.S. Center for Disease Control and the Missouri Head Injury Advisory Council which utilize and define the term.

Further, claims 17 and 24 have been amended to delete the word "about" from the definition of the molecular weight of the tau protein fragments.

In light of these amendments, it is submitted that the currently pending claims are fully supported by the specification and it is respectfully requested that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Paragraph 9. The Examiner has rejected the claims of the present application, under the second paragraph of 35 U.S.C. § 112, contending that the use of the phrase "in the form of an isoform of tau protein of SEQ ID NO:1" renders the claims ambiguous. Applicants have amended claim 14 in the manner suggested by the Examiner (claim 31 has been canceled). In light of that amendment, it is requested that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

Paragraph 10. Finally, the Examiner has rejected the claims, under 35 U.S.C. § 102(b), contending that they are anticipated by the disclosure of Vandermeeren et al. (WO 94/13795) which deals with the detection of Alzheimer's Disease. This rejection is respectfully traversed in view of the amendments to claim 14.

The claims in the present application relate to an assay to detect the presence and extent of "traumatic head injury." "Traumatic head injury" is an art-recognized term which is defined as an injury caused by a sudden insult to the brain or head (see the attached excerpt from the Missouri Head Injury Advisory Council). Such injuries would include, for example, a head hitting the steering wheel of a car in a car accident, a head being hit by a baseball bat, or a bullet wound to the head. It very clearly would not include Alzheimer's Disease which is not caused by a sudden insult to the head and therefore would not be considered a "traumatic head injury." If there is any doubt as to the correctness of that conclusion, the Examiner's attention is directed to the attached Missouri excerpt which states that a "traumatic head injury" is "not of a degenerative nature." Since Alzheimer's Disease is degenerative in nature

(see page 2, line 21 of the present application: "Alzheimer's Disease is a progressive degenerative disease . . ."), it clearly is not a "traumatic head injury." While Applicants are sure that when a patient gets Alzheimer's Disease it is emotionally traumatic for the patient's family, as the Examiner has pointed out, that does not make Alzheimer's Disease a "traumatic head injury" as that term is understood in the art. Since Vandermeeren et al. does not disclose or suggest any assays for traumatic head injuries, the present invention, as defined by the claims herein, is patentable over it. The same is true for newly-added claim 32 which relates to the detection of stroke (cerebrovascular accident) – again, not disclosed or suggested by the Alzheimer's Disease taught in Vandermeeren et al. Accordingly, it is respectfully requested that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Reconsideration and allowance of the present application is requested in view of the amendments and remarks made herein. Applicants have made a good faith effort herein to address all of the issues raised by the Examiner and place this application in form for allowance. if any additional issues need to be addressed prior to issuance of a notice of allowance, the Examiner is invited to call Applicants' attorney at the phone number below so that they can be worked out.

Respectfully submitted,
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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to The Assistant Commissioner for Patents, Box RCE, Washington, D.C., 20231, on May 13, 2002.

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CINlibrary/1179255.1

Appendix A
Marked Version Showing Changes Made

Claims 14, 17, and 24 are amended as follows:

Claim 14 (four times amended), A method of determining axonal damage in the [central nervous system] head of a patient suspected of having a traumatic [central nervous system] head injury, said method comprising the steps:

(a) obtaining a sample of cerebrospinal fluid from said patient;

(b) treating said sample of cerebrospinal fluid with at least one monoclonal antibody, said at least one monoclonal antibody having been raised against an axonally-derived [protein in the form of an isoform of] tau protein of SEQ ID NO:1;

(c) detecting the presence of said axonally-derived tau protein bound to said at least one monoclonal antibody; and

(d) comparing the amount of said axonally-derived tau protein bound to said at least one monoclonal antibody in step (c) to control samples from the group representing a normal undamaged axon state and those representing an axonal damage state.

Claim 17 (four times amended). A method according to Claim 14 wherein said axonally-derived tau protein is a fragment of said tau protein of SEQ ID NO:1 demonstrating an apparent molecular weight in the range of [about] 30 kDa to [about] 50 kDa.

Claim 24 (four times amended). A method according to Claim 23 wherein said axonally-derived tau protein bound to said at least one monoclonal antibody is a fragment of tau protein SEQ ID NO:1 which is detected through gel electrophoresis and which gives rise to an electrophoresis gel demonstrating multiple protein [bonds] bands with apparent molecular weights from [about] 30 kDa to [about] 50 kDa.

Claim 31 is canceled.

Claim 32 is added as follows:

Claim 32. (new) A method of determining axonal damage in the head of a patient suspected of having a cerebrovascular accident, said method comprising the steps of:

(i) obtaining a sample of cerebrospinal fluid from said patient;

(j) treating said sample of cerebrospinal fluid with at least one monoclonal antibody, said at least one monoclonal antibody having been raised against an axonally-derived tau protein of SEQ ID NO:1;

(k) detecting the presence of said axonally-derived tau protein bound to said at least one monoclonal antibody; and

comparing the amount of said axonally-derived tau protein bound to said at least one monoclonal antibody in step (c) to control samples from the group representing a normal undamaged axon state and those representing an axonal damage state.